Week 13 Clinical Endocrinology

**Bone & Mineral Metabolism in Health & Disease**

**HYPERcalcemia**

* Clinical manifestations:
* fatigue, depression, mental confusion, anorexia, nausea, vomiting, constipation, reversible renal tubular defects, ↑ urination, short QT interval, cardiac arrhythmias
* Ca >3.2 mmol/L – calcification: kidney, skin vessels, lungs, heart, stomach, renal insufficiency; Ca >3.7-4.5 mmol/L – coma, cardiac arrest
* Classification of causes:

Parathyroid-related, malignancy-related, vitamin D-related, associated w/ high bone turnover,

associated w/ renal failure

* Therapies for severe hypercalcemia

1. Most useful: Hydration w/ saline, forced diuresis (saline w/ loop diuretic)
2. Bisphosphanates – etidronate, pamidronate, zolendronate
3. Calcitonin
4. Special use: Phosphate, glucocorticoids, dialysis

**Hypocalcemia**

* Clinical manifestations:

Muscle spasm (carpopedal/laryngeal spasm, facial grimacing, convulsions, respiratory

arrest), ↑ ICP, papilledema, irritability, depression, psychosis, prolonged QT interval,

arrhythmia, intestinal cramps, chronic malabsorption, Chvostek’s or Trousseau’s sign

* Functional classification:
* PTH absent
* PTH ineffective - CRF, active vitamin D lacking (↓ dietary intake, sunlight; defective metabolism: anti-convulsant therapy; VDDR type I), active vitamin D ineffective (intestinal malabsorption; VDDR type II), pseudohypoparathyroidism
* PTH overwhelmed - severe, acute hyperphosphatemia (tumor lysis, ARF, rhabdomyolysis), osteitis fibrosa after parathyroidectomy

**Vitamin D deficiency**

* Clinical manifestations
* Mild – moderate: asymptomatic
* Long-standing: hypocalcemia (numbness, tingling, seizures), secondary HYPERparathyroidism, impaired mineralization of skeleton, proximal myopathy
* Associated with ↑ overall mortality rates, including cardiovascular causes
* Causes of impaired vitamin D action

1. Vitamin D deficiency - impaired cutaneous production, dietary absence, malabsorption
2. Accelerated loss of vitamin D - ↑ metabolism (barbiturates, phenytoin, rifampicin), impaired enterohepatic circulation, nephrotic syndrome
3. Impaired 25-hydroxylation - liver disease, isoniazid
4. Impaired 1 α-hydroxylation - hypoparathyroidism, renal failure, ketoconazole, 1 α-hydroxylase mutation, oncogenic osteomalacia, X-linked hypophosphatemic rickets
5. Target organ resistance - vitamin D receptor mutation, phenytoin

* Diagnosis
* Serum 25 (OH) D – most specific screening; deficiency <37 nmol/L (<15 ng/mL); optimum >80 nmol/L (>32 ng/mL)
* ↓ total & ionized calcium → ↑ PTH → ↑ alkaline phosphatase → ↓ phosphorus
* X-ray - ↓ cortical thickness, relative radiolucency of skeleton, pseudofractures (Looser’s zones) particularly in scapula, pelvis, femoral neck
* Treatment
* Vitamin D 800 IU/day; 1,25(OH)2D3 or calcitriol 0.25-0.5 μg/d; 1α-hydroxyvitamin D2 2.5-5 μg/d
* Calcium supplementation 1.5-2 g/day elemental Ca
* Monitor efficacy by serum & urinary calcium (100-250 mg/24/d)

**Primary HYPERparathyroidism**

* Generalized disorder of Ca, P, and bone metabolism due to ↑ PTH secretion
* Annual incidence = 0.2% in patients >60; prevalence >1%
* Etiology

1. Solitary parathyroid adenoma
2. Hereditary syndromes (e.g. MEN), multiple parathyroid tumors

* Signs & symptoms
* > 50% asymptomatic
* Kidney – deposition of calcium in parenchyma, recurrent nephrolithiasis
* Bone – osteitis fibrosa cystica (distinctive, rare), resorption of phalangeal tufts, irregular cortical outline (subperiosteal resorption)
* Neuromuscular – proximal muscle weakness, easy fatigability, atrophy of muscles
* GI – vague abdominal complaints, pancreatitis
* Diagnosis: ↑ PTH → ↑ calcium with ↓/normal phosphorus
* Treatment

1. Medical

Guideline for monitoring in asymptomatic primary hyperparathyroidism:

Serum Ca, Creatinine (clearance calculated), bone density (3 sites) - annually

1. Surgical

Guideline for surgery in asymptomatic primary hyperparathyroidism:

Serum Ca >1 mg/dL, Creatinine clearance calculated <60 mL/min, bone density T-score < -2.5 at any 3 sites, age <50

**Hypoparathyroidism**

* Etiology (PTH Absent) – Hereditary or acquired hypoparathyroidism, hypomagnesemia
* Signs & symptoms:
* Hereditary – more gradual onset, associated with other developmental defects
* Hypocalcemia, extraosseous (e.g. basal ganglia) calcification, extrapyramidal syndromes (choreoathetotic movements, dystonia), papilledema, ↑ ICP, lenticular cataract
* Treatment
* Vitamin D 40,000-120,000 U (1-3 mg)/d or calcitriol 0.5-1 μg/d
* Elemental calcium >1 g/d